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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,714	03/28/2006	Puthuparampil V Scaria	INTM/016	8393
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ROPS & GRAY LLP			WOLLENBERGER, LOUIS V	
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1211 AVENUE OF THE AMERICAS			ART UNIT	PAPER NUMBER
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			02/12/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/523,714	SCARIA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Louis Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 25 August 2008.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 46-64 is/are pending in the application.  
 4a) Of the above claim(s) 62-64 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 46-61 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 07 February 2005 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/28/08</u> .   | 6) <input type="checkbox"/> Other: _____ .                        |

**DETAILED ACTION**

*Status*

Applicant's reply filed 8/25/2008 is acknowledged.

Claims 46-64 are pending.

Claims 62-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 46-61 are examined herein.

*Priority*

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of prior-filed Provisional Application No. 60/401,029 fails to provide adequate written description support in the manner provided by the first paragraph of 35 U.S.C.

112 for claims 46-61 of the instant application. Specifically, written description support is not found therein for:

1. an siRNA that “comprises the sequence 5'-ucgagacccugguggacau-3' (SEQ ID NO: 6)”;
2. a composition comprising the siRNA comprising SEQ ID NO:6 and “an additional double-stranded nucleic acid molecule,” much less compositions thereof “wherein the additional double-stranded nucleic acid molecule decreases the expression of a VEGFR1 or VEGFR2 gene” or both VEGFR1 and VEGFR2; or
3. siRNA and/or nucleic acid molecule compositions comprising polymeric carriers or targeting moieties, such as any of those specifically recited in claims 53-61.

With regard to Point 1, support is found for an siRNA comprising 5'-ucgagacccugguggacauuu-3'. See page 6 of the priority document. This disclosure does not adequately convey possession of the genus of siRNAs comprising SEQ ID NO:6, as written in the claims. SEQ ID NO:6 is said to target VEGFA. With regard to Points 2 and 3, there is no disclosure in 60/401,029 generically describing or specifically exemplifying any compositions comprising the siRNA now claimed in claim 46 and any other double stranded nucleic acid molecule, much less those that specifically decrease the expression of either VEGFR1 or VEGFR2 or both, nor is there any description, technical or representative, of any polymeric carriers or targeting moieties that may be included in any such compositions. Instant claims 48-51 specifically embrace any double stranded nucleic acid molecule, including but not limited to

siRNAs targeted to VEGF or VEGF receptors. There is certainly no support in the instant priority document for the large genus of compositions now claimed. While the priority documents discusses use of an siRNA targeted to VEGFR2, there is no mention of any siRNA targeted to VEGFR1, nor is there any teaching suggesting or showing combinations of siRNAs targeted to both VEGF and VEGF receptors 1 and 2, also known in the art as Flt-1 and Flk-1/Kdr.

Accordingly, adequate written description support is not found in priority Application 60/401029 for the claimed siRNAs and compositions thereof as now claimed. As a result one of skill would not recognize Applicant was in possession of the inventions as now claimed at the time of filing of 60/401029. Should Applicant disagree with this finding, Applicant must, in replying to this Action point out with particularity by page and line number where support may be found.

For purposes of this examination, the earliest effective filing date of the claims 46-61 is considered to be that of PCT/US03/24587: 8/6/2003.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-51, and 53-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites the limitation “wherein the peptide comprises RGD amino acid sequence.” The term “RGD” is defined neither by the claims nor the specification and is not a recognized term of art. While the letters may be understood to denote the amino acids arginine, glycine, and aspartic acid, the symbols are not compliant with those approved by MPEP 2422 for defining an amino acid sequence; indeed, the lower case letters r and g have been reserved for nucleotide sequences. Furthermore, the term “RGD” in the claim may be confused with acronyms or abbreviations of the same. It is further noted that the claim as written appears to lack a definite or indefinite article (“an” or “the”) between “comprises” and “RGD.” Altogether, then, the metes and bounds of the claims are unclear, as the scope and meaning the limitation “comprises RGD amino acid sequence” is not adequately defined in the claims or the specification.

Correction is required.

For purposes of this examination, the claim is considered to be drawn to a peptide comprising an Arg-Gly-Asp sequence.

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Claim 47 is rejected as indefinite because of the recitation “a suitable carrier.” The claims do recite and the specification does not define what the carrier is to be suitable for. The term “suitable” reasonably implies the carrier must be of the right type or quality for a particular purpose or occasion. Yet neither the claims nor the specification provide the necessary information to adequately inform one of skill for what purpose or occasion the carrier is to right for. As a result, the limitation reasonably embraces any and every conceivable carrier for any purpose without limit. However, this interpretation raises doubt as to the claims scope in view of

the term "suitable," which, if it has no meaning and does not limit or further define the invention is either unnecessarily wordy and redundant, or, if intended to further limit the invention in a specific manner, is inadequately defined and therefore ambiguous. Dependent claims 48-51, and 53-61 are rejected therefor.

Clarification and/or correction is required.

***Claim Rejections - 35 USC § 112, first paragraph (new matter)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Instant claims 46-61 are not original claims. The claims were submitted by Applicant for the first time by amendment on 4/4/2008. In the Remarks attached therewith, Applicant points to several passages in the instant specification (10/523714) said to support the limitations recited in the claims. The passages have been fully reviewed, but fail to provide adequate written description support for the claims in the manner necessary under 35 USC 112, first paragraph.

For instance, while the instant application adequately describes the general use of cationic and hydrophilic polymers, including those that comprise histidine and lysine, in a composition comprising an siRNA, the application does not describe specific or general compositions comprising combinations of siRNAs and any additional double stranded nucleic acid molecule(s) (e.g., ribozymes, aptamers, decoys, plasmid DNA), including any additional siRNA, much less combinations of SEQ ID NO:6 or its equivalents and any particular double stranded nucleic acid molecules that inhibit one or both of VEGFR1 or VEGFR2. While Fig. 21 shows a data point for "mixed siRNAs," the specification does not identify the siRNAs in the mixture, or clearly point out which genes are targeted by the mixture. And aside from this data point, there is no other mention or description of any siRNA mixture, composition, combination, pool, or multi-target cocktail of any type, generally or particularly. Thus, the Examiner finds no support for the compositions of claims 48-52.

With regard to base claim 46, while support is found for an siRNA comprising 5'-ucgagacccugguggacauuu-3', said to have a UU overhang, support is not found for the genus of siRNAs comprising SEQ ID NO:6, as now claimed, with or without overhangs, with two or just one overhang, or of any length in the range recognized in the art to be embraced by the term siRNA, all of which are now embraced by claim 46. Instead Applicant has described one particular, 21-nucleotide siRNA having the sequence set forth at page 12 of the specification.

With regard to claim 58, while the specification adequately describes the use of a targeting "ligand," which may be a peptide comprising an RGD sequence (page 3), the specification does not describe targeting "moieties." The scope and meaning of the terms "ligand" and "moiety" are not considered to be identical or synonymous.

MPEP 2163, Section II, Part A, states in part that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed, *Wertheim*, 541 F.2d at 262, 191 USPQ at 96; however, with respect to newly added or amended claims, applicant should show support in the original disclosure for the new or amended claims. The purpose of the written description requirement is "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." MPEP 2138.05, I.

In the instant case, while Applicant has pointed to support, the support is inadequate for what is now claimed (MPEP 2163.04). Accordingly, one of skill would not recognize Applicant was in possession of the invention as now claimed at the time of filing.

Therefore, the instant claims as a whole are rejected for lack of written description support.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 46-55 and 60 are rejected under 35 U.S.C. 102(e) as being anticipated by Tolentino et al. (US 7,148,342, as supported by US Provisional Application 60/398417, filed 7/24/2002).

Citing from US Provisional Application 60/398417, Tolentino et al. taught siRNAs for inhibiting vascular endothelial growth factor and its receptors, Flt-1 and Flk-1/KDR, also called VEGF receptor 1 and VEGF receptor 2, respectively (pages 1-8). Pharmaceutical compositions are disclosed at pages 3 and 4. It is taught that agents such as siRNAs that selectively decrease VEGF and/or VEGF receptor 1 and VEGF receptor 2 levels may be used to treat malignancies and other angiogenic diseases (page 2 of 9; see also Abstract). For example, at page 3 it is taught a pharmaceutical composition may be prepared by mixing one or more short RNA duplexes according to the invention with a physiologically acceptable excipient, and optionally additional substances, additives, or auxillaries. Such substances, additives, or auxillaries might reasonably be considered to include any of the polymeric or polycationic delivery reagents described at pages 7 and 8, including polylysine. Absent a clear limiting definition, which is not currently found, polylysine is considered to be an amino acid copolymer, peptide, targeting moiety, and hydrophilic polymer, within the scope of claims 55, 57, 58 and 60. Several other amphiphilic polymers are also disclosed at pages 7 and 8, which similarly also fulfill the requirements of claim 60.

In one embodiment, Tolentino et al. taught the siRNA of their invention may be specifically targeted to the site in VEGF corresponding to the sequence tcgagaccctggatcat, which is identical to the site targeted by the siRNA claimed in claim 46, as defined by instant SEQ ID NO:6 (see site #3 at page 5 of Tolentino et al.).

Accordingly, Tolentino et al. taught the siRNA specifically claimed in claim 46 as well as compositions comprising said siRNA for inhibiting VEGF. Additionally, Tolentino et al. taught combining said siRNA with other siRNAs directed to VEGF and its receptors VEGFR1 and 2 to

effectively treat malignancies and angiogenic disorders associated with the expression and activities of VEGF and its receptors 1 and 2.

Therefore, Tolentino et al. anticipated the instantly claimed siRNA and compositions thereof.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 56-59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tolentino et al. (US 7,148,342, as supported by US Provisional Application 60/398417, filed 7/24/2002) as applied to claims 46-55 and 60 above, and further in view of Woodle et al. (WO 01/49324) and Mixson (WO 01/47496).

Tolentino et al. is relied on for the reasons given above.

Tolentino et al. did not expressly teach targeting moieties, amino acid copolymers comprising histidine and lysine, peptides comprising an RGD amino acid sequence, or polyethylene glycol.

Woodle et al. taught polyethylene glycol-containing “colloidal vectors” comprising one or more defined chemical reagents for enhancing the delivery of nucleic acids into tissues and cells (pp. 1-130; page 9 through 10, for example). The nucleic acid “payload” delivered with said PEG-containing compositions may be any DNA or RNA therapeutic nucleic acid, including any antisense RNA, ribozyme, or double stranded RNA that inhibits gene expression (page 7, 16, and 18). The delivery agents may be formulated as pharmaceutical compositions (page 5). With regard to claims 57 and 58, the vectors may comprise a fusogenic or targeting moiety (page 5, for example), such as any of those peptides or ligands listed at pages 46-50, including and RGD peptide (page 47). For instance at page 130, Woodle et al. specifically describe compositions comprising an RGD peptide with and without PEG.

Mixson taught histidine-lysine copolymers for enhancing the delivery of virtually any DNA or RN nucleic acid molecule into cells and tissues in vitro and in vivo for research and

therapeutic purposes (pp. 1-31). The copolymers are disclosed for use in combination with other non-viral delivery agents.

Accordingly, the prior art suggested the use of histidine/lysine copolymers, targeting moieties, RGD peptides, and polyethylene glycol-containing compositions for the enhanced and targeted delivery of DNA and RNA therapeutic nucleic acids into cells *in vitro* and *in vivo*. It would therefore have been *prima facie* obvious for one skill to make and use such compositions with any siRNA or siRNA combination to similarly enhance the delivery of said siRNA into a cell and thereby more effectively inhibit the target gene. Given the detailed direction and guidance and numerous representative examples provided by Woodle et al. and Mixson, one of skill would have had reasonably predicted such compositions could be used successfully with short interfering double stranded RNAs.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 46-61 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25-37 of copending Application No. 10/286956 in view of Tolentino et al. (US 7,148,342, as supported by US Provisional Application 60/398417, filed 7/24/2002).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting application claims a method for reducing VEGFR2 expression in a subject using a synthetic vector comprising an siRNA targeted to VEGFR2. In certain embodiments the vector may comprise one or more additional siRNA molecules, wherein at least one of the molecules targets VEGFR2; a cationic polymer; a histidine-lysine copolymer; a hydrophilic polymer such as PEG; and a targeting moiety such as an RGD peptide.

While the conflicting application does not expressly claim the combination of VEGF and VEGFR1 and R2 siRNAs of the instant application, these combinations are reasonably suggested by the conflicting application in view of claim 27 and by the prior art, as shown by Tolentino et al. who expressly taught such combinations for more effectively treating malignancies.

Therefore, one of ordinary skill in the art would conclude that the invention defined in the claims at issue is anticipated by, or would have been an obvious variation of, the invention defined in a claim in the conflicting application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Prior art made of record but not currently relied on***

The following prior art is made of record and is not relied upon, but is considered pertinent to applicant's disclosure.

Dias et al. (2001) *Proc. Natl. Acad. Sci.* 98:10857-10862 taught that agents that block the VEGF/VEGFR2 pathway inhibit tumor cell growth, and may be effective against leukemia cell growth.

Strawn et al. (1996) *Cancer Res.* 56:3540–3545 taught the correlation between Flk-1 (VEGFR1) and tumor cell growth.

Arbiser et al. (2000) *Am. J. Pathol.* 156:1469-1476 taught a correlation between the expression of VEGFR1 and 2 and angiosarcoma.

Uchida et al. (US Patent 6,150,092) As shown by the alignment below, Uchida et al. taught a 20-nucleotide antisense oligonucleotide targeted to a site in VEGF identical to instant SEQ ID NO:6. As shown by the data shown in Table 1, column 12, the antisense oligonucleotide is shown to be highly inhibitory.

```
RESULT 3
US-08-765-340-43/c
; Sequence 43, Application US/08765340
; Patent No. 6150092
; GENERAL INFORMATION:
;   APPLICANT: UCHIDA, K.,
;   APPLICANT: UCHIDA, T.,
;   APPLICANT: TANAKA, Y.,
;   APPLICANT: MATSUDA, Y.,
;   APPLICANT: KONDO, S.
;   TITLE OF INVENTION: AN ANTISENSE NUCLEIC ACID
;   TITLE OF INVENTION: COMPOUND
;
; CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: US/08/765,340
;   FILING DATE: 23-DEC-1996
; PRIOR APPLICATION DATA:
;   APPLICATION NUMBER: JP 145146/94
;   FILING DATE: 27-JUN-1994
; PRIOR APPLICATION DATA:
;   APPLICATION NUMBER: JP 311130/94
;   FILING DATE: 21-NOV-1994
;
; INFORMATION FOR SEQ ID NO: 43:
; SEQUENCE CHARACTERISTICS:
;   LENGTH: 20 base pairs
;   TYPE: nucleic acid
;   STRANDEDNESS: single
;   TOPOLOGY: linear
;   MOLECULE TYPE: other nucleic acid
;   DESCRIPTION: /desc = "synthetic DNA"
US-08-765-340-43

Query Match          100.0%...SRRRE 19; DB 3; Length 20;
Best Local Similarity 78.9%; Pred. No. 54;
Matches 15; Conservative 4; Mismatches 0; Indels 0; Gaps 0;

Qy      1 UCGAGACCCUGGUGGACAU 19
       :|||||||:||:|||||:
Db      19 TCGAGACCCCTGGTGACAT 1

```

### *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/  
Examiner, Art Unit 1635  
February 5, 2009